Universitätsspital Zürich
Departement für Frauenheilkunde
Vorsteher: Prof. Dr. med. D. Fink
Abteilung Geburtshilfe
Leiter: Prof. Dr. med. R. Zimmermann

Arbeit unter der Leitung von Prof. Dr. med. J. Wisser

Volumenmessung der analen Sphinktermuskelatur

Vergleich eines Patientenkollektivs nach primärer Sectio mit einem Patientenkollektiv nach vaginal operativer Entbindung

Inaugural – Dissertation

Zur Erlangung der Doktorwürde der Medizinischen Fakultät der Universität Zürich

Vorgelegt von
Leila Sultan

Introduction:

Over the last twenty years obstetricians discussed about the consequences of different delivery modes for long term maternal morbidity. Currently, caesarean section rates in Canada and the United States are close to 25% and over 20% in England, Wales, and Northern Ireland[20]. In the past few years indication as well as accomplishment of a caesarean section has been increased enormously. Certainly there are various reasons for it but one of the most controversial subjects seems to be urinary and faecal incontinence in women after vaginal delivery. There are several studies trying to find correlation between delivery mode and incontinence, but it seems, that there is still a lack of information to completely explain the reason for incontinence. A very common cause for anal incontinence in women is thought to be anal sphincter injury sustaining during vaginal delivery [1]. There for vaginal delivery were scrutinized the first time by Sultan *et. al*. Changes of the anal sphincter during pregnancy and especially after vaginal delivery need to be well investigated. The following study is a pilot study to introduce a new technique for processing ultrasound data. To gain more detailed information about the internal anal sphincter the 3D volume sonography could be helpful. Processing ultrasound data with the 3D Slicer is a new approach to provide a better insight into the pelvic floor anatomy as to see for example whether morphologic changes in the internal anal sphincter are reflected in volume changes. To establish this new method in daily clinical pratice the inter- and intrarater variability needs to be investigated.

Methods:

For a previous study [2] 3D-ultrasound-volumes were obtained post partum from 237 primiparous women in the age between 17 an 42 years. 18 of these women were randomly selected for our study. We examined 10 woman after primary caesarean section where no pelvic and especially no sphincter trauma was expected (Group 1) and 8 woman after vaginal delivery (3 forceps, 5 vacuum) (Group 2). The mean body-mass-index (BMI) right before confinement was 28,93 kg/m^2 (range 25,48 to 36,73) in Group 1 and 28,35 kg/m^2

(range 20,94 to 41,66) in Group 2. The local institutional review board approved the protocol of this study and all patients gave informed consent.

Each patient underwent a transvaginal and a transrectal sonographical examination with a 3D-ultrasound-unit between the 2nd and 5th day after delivery. To perform the ultrasound examination, a 3D-ultrasound equipment Voluson 530D, Kretztechnik, Zipf, Austria was used. The examination was performed in lithotomy position, with an empty bladder and the patient at rest. Volumes of the undistended internal anal sphincter muscle were taken with a 7,5 MHz transvaginal probe placed at the posterior frenulum of labia minora. The data sets have an isotropic resolution of 0,3 mm in each spatial direction. The data acquisition was carried out by one of the authors (JW) carefully in order not to compress the anatomy in the considered anatomical region. Structures of interest in our study were the internal anal sphincter and the mucosa. These structures can be very well identified with 3D ultrasound. The most proximal point of the internal anal sphincter was defined as the first level at which the internal anal sphincter was seen as a clear hypoechogenic ring and the most distal point as the level where the internal anal sphincter was last seen as a complete ring. In order to create 3D models of the internal anal sphincter, a 3D modelling software were used *(3D Slicer, MIT Artificial Intelliegence Lab and the SPL at BWH, Harvard Medical School)*. Before starting the modelling process, the ultrasound data sets need to be transferred in a readable format for the 3D Slicer. Therefore it has to be reformatted into parallel slices in RAW format, being stored originally in proprietarian cartesian volume data format with an separate software solution (CS). After reformatting, *3D Slicer* is able to read the ultrasounds volumes and one can see slide by slide. How the 3D Slicer operates is very well described by *Hoyte* [3] Every volume set per patient counts about 220 – 250 slices which can be edit in a axial, coronal or sagittal view, as well as any combination of views that the examiner desires. The surface models can be viewed and measured in the same program.

The same volume sets were edited from three different examiners, where each examiner segmented each volume of a patient twice, blinded to previous calculation and in separate occasions approximately 3 month apart. A statistical approach as suggested by Bland and Altman [4] was used in a modified way to confirm reproducibility of this new method. As it is described the actual difference between each set of individual measurements were calculated for two measurements made by one examiner as well as for those between the three examiners to asses intra - and interobserver variability. In order to compare the influence to the volume of the internal anal sphincter in different delivery modes, a statistical method by *Rousson et al* [5] was used. Both outcomes (sphincter and mucosa) were measured twice on each patient by three different raters, resulting in six measurements per patient.

Results

Reliability of measurements was assessed using intraclass correlation calculated from variance components in a model with factors "patient" and "rater" as random-effects and with a factor "group" as fixed-effect. Comparison between the groups with respect to both outcomes was assessed in an ANOVA for repeated measurements, which is equivalent to consider the average of the six measurements per patient in a two-sample t-test.

a) Reliability of sphincter

Variance components for the patient-effect, the rater-effect and the error term were equal to 0.245, 0.087 and 0.040, respectively. This resulted in an intraclass correlation of

$$0.245/(0.245+0.087+0.040)=0.659.$$

Thus, about two third (65.9%) of the variability among the measurements was not due to measurement errors. The systematic error among the raters was responsible for

$$0.087/(0.245+0.087+0.040)=23.4\%$$

of the variability, which is not negligible. Finally, measurement errors not due to this rater bias accounted for

$$0.04/(0.245+0.087+0.040)=10.8\%$$

of the variability. Limits of agreement proposed by Rousson, Gasser and Seifert (2002) for the differences between two arbitrary measurements made on a same subject (which are a generalization of Bland and Altman's limits of agreement) were

[-2*sqrt(2*(0.087+0.040));+2*sqrt(2*(0.087+0.040)]=[-1.008;+1.008].

Thus about 95% of the differences between two measurements of sphincter made on a same patient were smaller on magnitude than 1.

b) Reliability of mucosa

Variance components for the patient-effect, the rater-effect and the error term were equal to 0.247, 0.000 and 0.066, respectively. This resulted in an intraclass correlation of

0.247/(0.247+0.000+0.066)=0.789.

This means that 78.9% of the variability among the measurements was not due to measurement errors. Thus, measurement errors accounted for

0.066/(0.247+0.000+0.066)=21.1%

of variability. Note that there was practically no systematic difference among the raters for this outcome. Limits of agreement were *(see Fig. 1+2)*

[-2*sqrt(2*(0.000+0.066));+2*sqrt(2*(0.000+0.066)]=[-0.727;+0.727].

Thus about 95% of the differences between two measurements of mucosa made on a same patient were smaller on magnitude than 0.7. *(see Fig. 3+4)*

c) Comparison of groups

Averages of the six sphincter measurements were on average larger in the primary caesarean section group than in the vaginal operative group (1.33 vs. 1.03) but this difference was not statistically significant (p=0.21). Both groups were very similar with respect to averages of the six mucosa measurements, which were on average 1.83 in the primary caesarean section group and 1.77 in the vaginal operative group. Here also, no statistical significance could be found (p=0.81)[5].

Discussion

Editing the 3D Volume sonography data, including the 3D – Visualization give us a new approach to get a better understanding about the anatomy of the pelvic floor, especially the internal anal sphincter. More over we wanted to establish a new method, which allows us to obtain 3D models of different anatomical structures like mucosa and the internal anal sphincter. The 3D Slicer makes it possible that we are able to work with the models, we could measure the real volume and we could more over reveal for example small tears or injuries *(see Pict.1).* As far as we know, no such volume measurements are existing, using 3D volume sonography and processing the data with the 3D Slicer. In addition the 3D Slicer give us the opportunity to edit directly on the 3D-Volume sonography volume block slice by slice free hand without any adaption of greyscales which is necessary in contrast to the MRI [7]. Using 3D Slicer for 3D- Ultrasound data is a low-cost application where we could gain very detailed information about the anal-canal and the neighbouring tissue without the need of sophisticated overlaying filtering techniques.

There are many statistical analyses that might be used to measure the reproducibility of one method, and the results may differ widely depending on the number of the various statistical analyses, which were used. Based on a generalization of *Bland and Altmann [4]* in our study the reliability of sphincter-measurements was 0.659. About 95% of the differences between two measurements of internal anal sphincter made on a same patient were smaller on magnitude than 1. That shows, that our method is reproducible but has a moderate reliability. One of the reasons for the moderate reproducibility might be the difficulty to define the lengths of the anal sphincter muscle. Modelled on the internal anal sphincter, we got very similar, even better result for the mucosa, which was 0.789. For the measurements of mucosa there was practically no systematic difference among the raters for this outcome.

Discrepancies in intraobserver and interobserver variability in volume measurements and segmentation are probably related to the experience of the investigator. *Gregory et al* [8] described a similar method and showed also a decent reproducibility. Although 3D volume sonography is a widely used technique, only a few studies have reported on reproducibility of 3D volume sonography measurements, and the results differ [9-12]. To our knowledge no study looked for the volume of the internal anal sphincter, measured and reconstructed by the 3D Slicer. More over no studies compare the influence of different delivery modes to the anatomy of the internal anal sphincter volume. The few studies, as far as we know, concerning about sphincter volume measurement used always the anorectal access. We used on purpose the transvaginal access in order not to compress or dilate the anal sphincter muscles. Endoanal MRI is also an accepted technique for evaluating the anal sphincters [12,13]. However, interobserver agreement for assessing the integrity of sphincter muscle is moderate with this technique [14]. But potentially clinically relevant measures of muscle mass and morphology are not limited to the sphincter muscles. Detailed studies of representative morphologic changes of levator ani muscles in women with pelvic floor disorders were published by *Hoyte et al [3]*, also using the 3D Slicer.

The comparison of the two different delivery modes shows, that there is a slight difference between these groups. Compared to the primary caesarean section group, the internal anal sphincter was thinner after vaginal operative delivery. However we could not verify a statistical significance ($p=0.21$), maybe because of the moderate reproducibility and the limited number of patients.

A long second stage of labour, obesity and high birthweight seemed to be risk factors for pelvic floor trauma [15,16]. Caesarean section appears to be protective, although protection was only complete in women delivered electively [17]. The authors of this study also concluded that vaginal delivery, or even the attempt at vaginal delivery causes partial denervation of the pelvic floor in most women. These results correlates with our findings: a partial dernervation of the pelvic floor during vaginal delivery or even more traumatic, a vaginal operative delivery leads to a loss of internal anal sphincter volume. But correlation between sphincter volume and function still needs to be investigated and discussed in further studies [18]. *Allen et al* [17] were able to correlate neuropathic changes with function. They saw a reduction in mean maximal perineometric contraction pressure from 15.6 cm H_2O to 10.1 cm H_2O at the postpartum visit, confirming that the neurophysiological changes observed on CN-EMG were associated with impaired levator function. Concentrating on sphincter muscle *Snooks et al* [15] describes in studies spanning more then 5 years an increase of pudendal nerve terminal motor latencies measured at external anal sphincter after vaginal delivery. Forceps delivery, length of second stage and birthweight were the main risk factors for pudendal nerve damage [16]. In a follow – up study 5 years later the authors showed that pudendal nerve injury persisted and getting even worse over the time. They also found an association between abnormal fibre density and stress urinary incontinence and anal incontinence, although numbers were low [19]. Surprisingly a recently published study shows, that there is no correlation between anal sphincter volume and faecal incontinence [18].

It has to be mentioned that during our work we find out, that our new method, editing the 3D ultrasound volume block with the 3D Slicer takes quite a long time to finally get a thorough 3D sphincter model. Our experienced examiner needed approximately *5-6 hours* segmenting the data of one patient. Even though there is a learning curve in segmenting the data, non of the examiner was able to be faster then 5 hours.

For a broader implementation based on our results of this pilot study we need further improvements of accuracy and applicability of this method. It is quite difficult to obtain standardized measurements of the anal sphincter especially in the longitudinal direction, which results in an increase of variability. The accuracy of the measurements could be further enhanced with higher resolution in ultrasound data by adapted ultrasound equipment. If we could gain high-resolution volume samples, rendering systems would be much more precise. In addition the comparison of muscle *volumes* should be reconsidered. A comparison of the surface for example of the 3 D models with a specifically customized tool, might provide more exactness of the anatomical structures. Just the *visualisation* of the anal sphincter might be more important then the volume. *(See pict 2)*

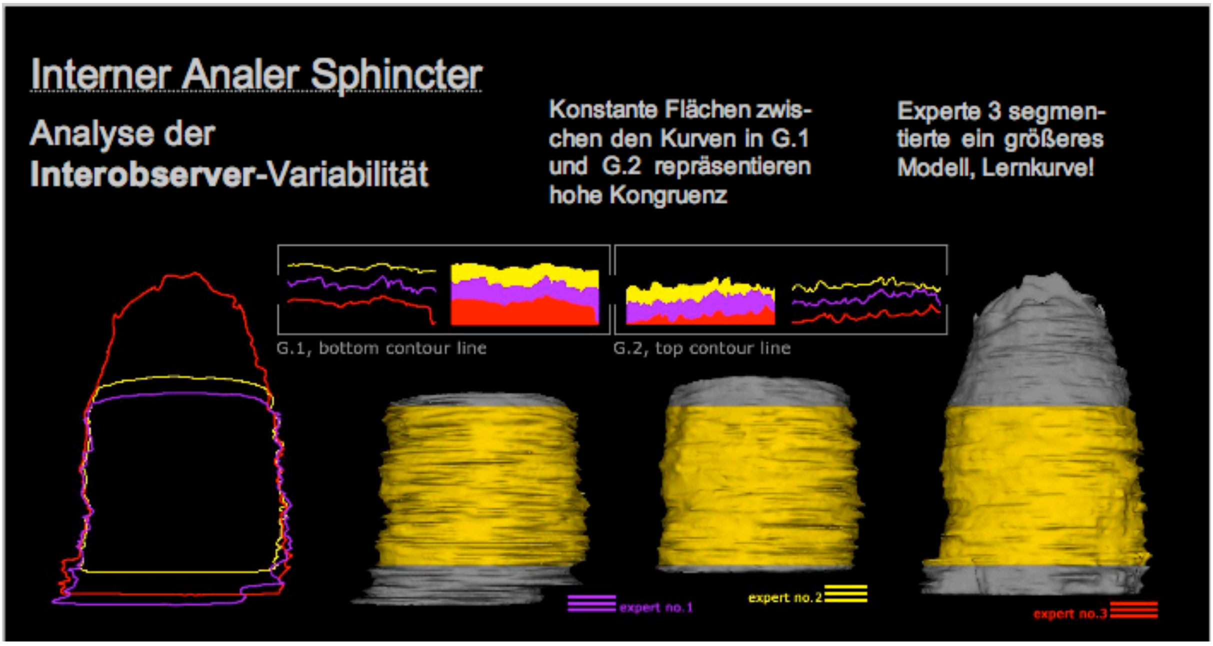
Our new method offers further insight into the pelvic floor anatomy, eminently anal sphincter morphology and disorders of the sphincter muscle. Up to now an automatic segmentation is still not possible. So it should be considered to use this method only in special selected cases for example for elective operative sphincter repairs and for a preoperative planning setting.

Our method could turn out to be an important tool for these applications if the above mentioned developments could be realized. One of the aims of our future studies beside technical improvements will be to collect as much data as needed to define a gold standard and analyse the interobserver variability for 3D Volume sonography data which make an automatic segmentation possible for the 3D Slicer. *(see pict. 2+3)*

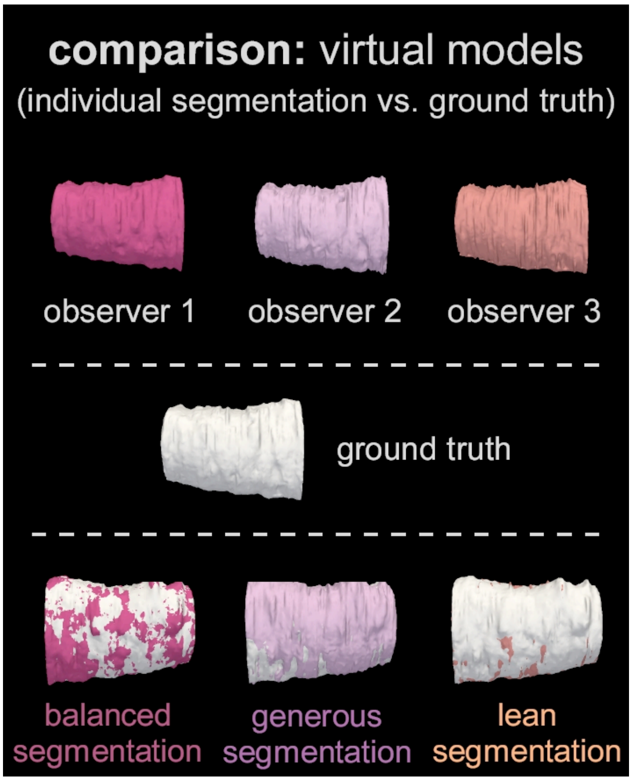
Anhang

1. Sultan AH, Kamm MA, Hudson CN, Thomas JM, Bartram CI: Anal-sphincter disruption during vaginal delivery. N Engl J Med 1993;329:1905-1911.
2. Ochsenbein N, Kurmanavicius J, Huch R, Huch A, Wisser J: Volume sonography of the pelvic floor in nulliparous women and after elective cesarean section. Acta Obstet Gynecol Scand 2001;80:611-615.
3. Hoyte L, Jakab M, Warfield SK, Shott S, Flesh G, Fielding JR: Levator ani thickness variations in symptomatic and asymptomatic women using magnetic resonance-based 3-dimensional color mapping. Am J Obstet Gynecol 2004;191:856-861.
4. 'Bland JM, Altman DG: Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;1:307-310.
5. Rousson V, Gasser T, Seifert B: Assessing intrarater, interrater and test-retest reliability of continuous measurements. Stat Med 2002;21:3431-3446.
6. Wisser J, Schar G, Kurmanavicius J, Huch R, Huch A: Use of 3D ultrasound as a new approach to assess obstetrical trauma to the pelvic floor. Ultraschall Med 1999;20:15-18.
7. Verhey JF, Wisser J, Keller T, Westin CF, Kikinis R: Rigid overlay of volume sonography and MR image data of the female pelvic floor using a fiducial based alignment--feasibility due to a case series. Comput Med Imaging Graph 2005;29:243-249.
8. Gregory WT, Boyles SH, Simmons K, Corcoran A, Clark AL: External anal sphincter volume measurements using 3-dimensional endoanal ultrasound. Am J Obstet Gynecol 2006;194:1243-1248.
9. Nielsen MB, Hauge C, Rasmussen OO, Sorensen M, Pedersen JF, Christiansen J: Anal sphincter size measured by endosonography in healthy volunteers. Effect of age, sex, and parity. Acta Radiol 1992;33:453-456.
10. Enck P, Heyer T, Gantke B, Schmidt WU, Schafer R, Frieling T, Haussinger D: How reproducible are measures of the anal sphincter muscle diameter by endoanal ultrasound? Am J Gastroenterol 1997;92:293-296.
11. Gold DM, Halligan S, Kmiot WA, Bartram CI: Intraobserver and interobserver agreement in anal endosonography. Br J Surg 1999;86:371-375.
12. Hussain SM, Stoker J, Lameris JS: Anal sphincter complex: endoanal MR imaging of normal anatomy. Radiology 1995;197:671-677.
13. Beets-Tan RG, Morren GL, Beets GL, Kessels AG, el Naggar K, Lemaire E, Baeten CG, van Engelshoven JM: Measurement of anal sphincter muscles: endoanal US, endoanal MR imaging, or phased-array MR imaging? A study with healthy volunteers. Radiology 2001;220:81-89.
14. Malouf AJ, Halligan S, Williams AB, Bartram CI, Dhillon S, Kamm MA: Prospective assessment of interobserver agreement for endoanal MRI in fecal incontinence. Abdom Imaging 2001;26:76-78.
15. Snooks SJ, Swash M, Mathers SE, Henry MM: Effect of vaginal delivery on the pelvic floor: a 5-year follow-up. Br J Surg 1990;77:1358-1360.
16. Snooks SJ, Swash M, Henry MM, Setchell M: Risk factors in childbirth causing damage to the pelvic floor innervation. Int J Colorectal Dis 1986;1:20-24.
17. Allen RE, Hosker GL, Smith AR, Warrell DW: Pelvic floor damage and childbirth: a neurophysiological study. Br J Obstet Gynaecol 1990;97:770-779.
18. West RL, Felt-Bersma RJ, Hansen BE, Schouten WR, Kuipers EJ: Volume measurements of the anal sphincter complex in healthy controls and fecal-incontinent patients with a three-dimensional reconstruction of endoanal ultrasonography images. Dis Colon Rectum 2005;48:540-548.
19. Snooks SJ, Badenoch DF, Tiptaft RC, Swash M: Perineal nerve damage in genuine stress urinary incontinence. An electrophysiological study. Br J Urol 1985;57:422-426.
20. Royal College of Obstetrics and Gynaecology Clinical Effectiveness Support Unit. *The national sentinel caesarean section audit report*. London: RCOG Press, 2001.

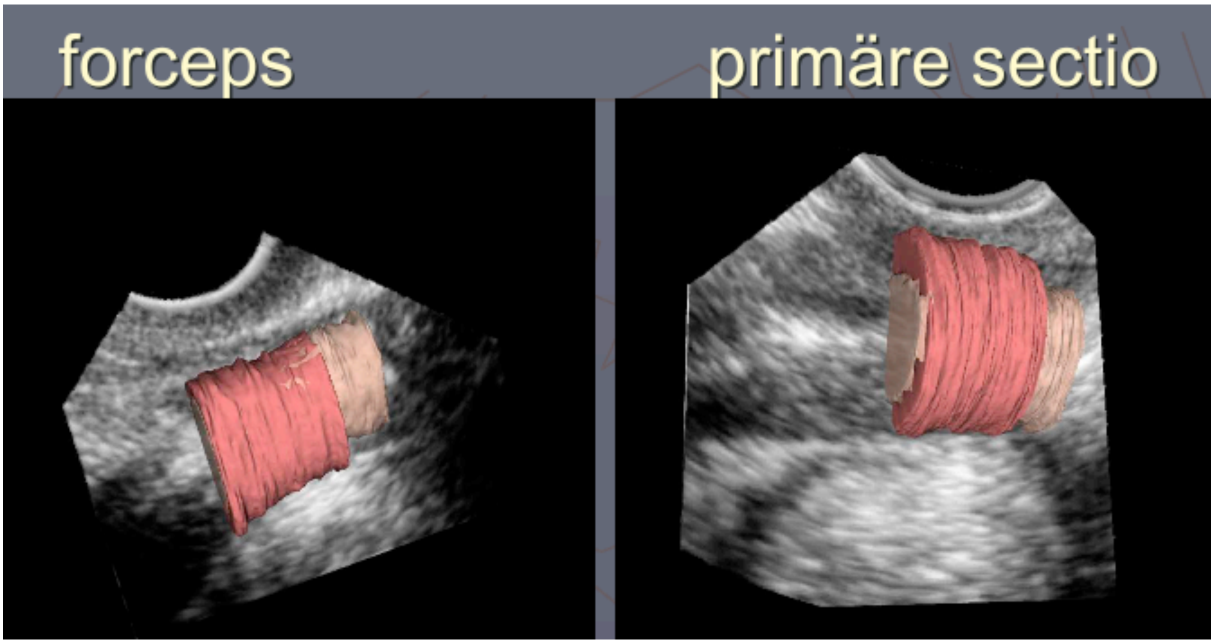
Bilder.



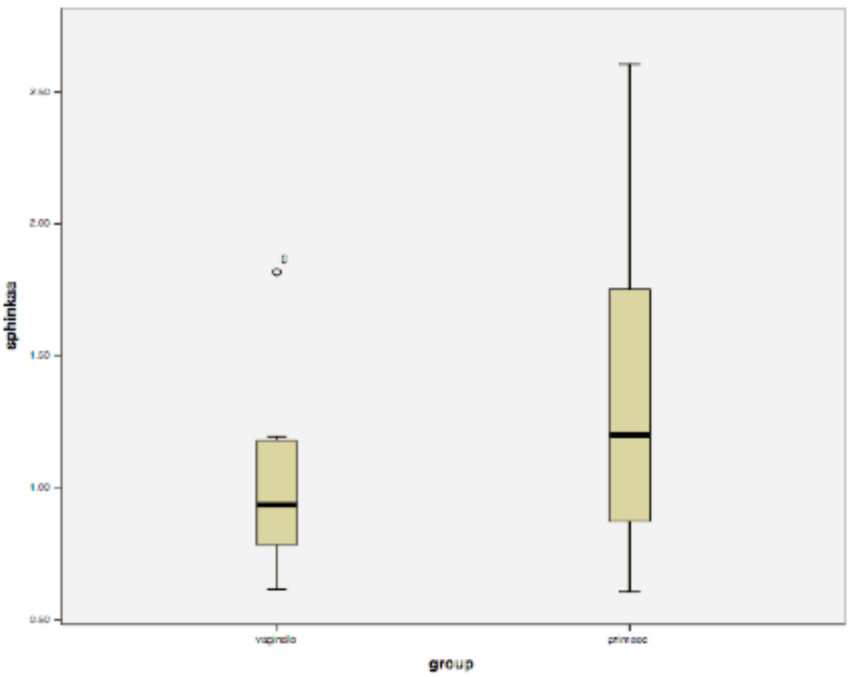
Interner Analer Sphincter
Analyse der
Interobserver-Variabilität
Konstante Flächen zwis-
chen den Kurven in G.1
und G.2 repräsentieren
hohe Kongruenz
Experte 3 segmen-
tierte ein größeres
Modell, Lernkurve!
G.1, bottom contour line
G.2, top contour line
expert no.1
expert no.2
expert no.3



comparison: virtual models
(individual segmentation vs. ground truth)
observer 1
observer 2
observer 3
ground truth
balanced segmentation
generous segmentation
lean segmentation


forceps
primäre sectio

sphinkaa



mucosaaa